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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/695,578	10/27/2003	Scott A. Waldman	100051.10611	5382

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EXAMINER	
AEDER, SEAN E	
ART UNIT	**PAPER NUMBER**
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/695,578	**Applicant(s)** WALDMAN, SCOTT A.	
	Examiner SEAN E. AEDER	**Art Unit** 1642	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 2/12/09 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *47,48,50-53,55 and 56*.
   Claim(s) rejected: *24,25,28-35 and 38-46*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Sean E Aeder/
Primary Examiner, Art Unit 1642

Continuation of 5. Applicant's reply has overcome the following rejection(s): The rejection of claims 47, 48, 50-53, 55, and 56 Under 35 U.S.C. 112, first paragraph.

Continuation of 11. does NOT place the application in condition for allowance because: Claims 50 and 55 are objected to for failing to further limit the claims from which they depend. The claims from which claims 50 and 55 depend require that "said protein comprises amino acids 24-454 of SEQ ID NO:2. Proper correction is required.

Claims 24,25,28-35 and 38-46 remain rejected under 35 U.S.C. 112, first paragraph, for failing to comply with the enablement requirement for the reasons stated in the Office Action of 7/10/08, for the reasons stated in the Office Action of 1/12/09, and for the reasons set-forth below.

The specification, while being enabling for methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of an expression vector comprising a nucleic acid sequence encoding amino acids 24-454 as set-forth in SEQ ID NO:2, the specification does not reasonably provide enablement for methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of an expression vector comprising a nucleic acid that encodes just any extracellular domain of just any human guanylyl cyclase C protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required are summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.
The instant claims are broadly drawn to methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of just any composition comprising a nucleic acid molecule that encodes just any epitope of just any human guanylyl cyclase C protein. This includes methods wherein nucleic acids are administered in compositions that would not generate polypeptides and would not produce a therapeutic or prophylactic response. Further, this is drawn to methods wherein nucleic acids comprising just any human guanylyl cyclase C protein epitope, including nucleic acids consisting of transmembrane epitopes or nucleic acids consisting of cytoplasmic epitopes, are administered. Further, this is drawn to methods wherein nucleic acids comprising just any epitope of any receptor found on colorectal cells which binds to ST are administered.

The specification prophetically describes methods of treating an individual who has metastasized colorectal cancer or an individual who is susceptible to metastasized colorectal cancer with a vaccine comprising a nucleic acid molecule encoding at least one epitope of human ST receptor protein (page 11-12, in particular).

Further, the specification discloses the terms “ST receptor” and “guanylin cyclase C” are interchangeable and are broadly meant to refer to receptors found on colorectal cancer cells which bind to ST (see page 7). Further, the specification discloses the polypeptide set-forth as SEQ ID NO:2 is an ST receptor (see page 13). The specification further discloses that the extracellular region of SEQ ID NO:2 is from about amino acid 24 to about amino acid 454 of SEQ ID NO:2 (page 13). The specification further discloses that the transmembrane region of SEQ ID NO:2 is from about amino acid 455 to about amino acid 475 of SEQ ID NO:2 (page 13). The specification further discloses the cytoplasmic region of SEQ ID NO:2 is from about amino acid 476 to about amino acid 1093 of SEQ ID NO:2 (page 13).
It is further noted that the Reply of 5/2/08 states that “guanylyl cyclase C" is misspelled in the instant specification as “guanylin cyclase C”.
It is further noted that the specification does not limit the term “guanylyl cyclase C" (disclosed as “guanylin cyclase C”) to a particular SEQ ID NO. Rather, at lines 17-20 on page 7, the specification provides the following broad definition:

"As used herein, the term "ST receptor" and "guanylin cyclase C" are interchangeable and meant to refer to the receptors found on colorectal cells, including local and metastasized colorectal cancer cells, which bind to ST."

Said definition is used to define the meaning of "guanylyl cyclase C" in the claims, as Applicant is entitled to be his or her own lexicographer (see MPEP 211.02). Therefore, the term “guanylyl cyclase C" is interpreted to encompass a genus comprising ALL receptors found on colorectal cells which bind to ST.

The Declaration of Scott Waldman demonstrates methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of a viral vector comprising a nucleic acid sequence encoding the first 430 amino acids of a guanylyl cyclase C protein. Said first 430 amino acids comprise extracellular binding domain regions of a guanylyl cyclase C. It appears SEQ ID NO:2 is the guanylyl cyclase C protein of the Declaration. The Declaration further describes a study wherein said guanylyl cyclase C protein is taught to be expressed on colorectal tumor cells and is an ideal target for immunotherapy. However, the Declaration does not address whether just any receptors found on colorectal cells which bind to ST would be ideal targets for immunotherapy.

Further, those of ordinary skill in the art recognize that treatment in vivo is not predictive. The instant situation is analogous to that of In re Brana (34 U.S.P.Q. 2d 1436, 1440 (Fed. Cir. 1995)). A review of In re Brana reveals an application that claimed a chemical compound for treating a cancer, wherein the chemical compound was structurally similar to known compounds that have known in vivo use to treat tumors, and more importantly, Applicant provided in vivo data that the claimed compound could treat tumors in mice, hence it was ruled that the claimed compound was enabled for treating tumors. In the instant application, expression vectors comprising nucleic acids encoding polypeptides comprising extracellular domains of just any receptors found on colorectal cancer cells which bind to ST are not known in vivo to give rise to a therapeutic effect. In view of In re Brana, Examiner asserts that successful use of in vivo mouse models of colon cancer enables compositions for specific therapeutic effects in humans and does not require human clinical testing.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to methods for treating individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer comprising administering a therapeutically effective or prophylactically effective amount of an expression vector comprising a nucleic acid molecule that encodes just any extracellular region of just any protein that binds ST on colorectal cancer cells, and Applicant has not enabled said method because it has not been shown that administering just any expression vector comprising a nucleic acid molecule that encodes just any extracellular region of just any protein that binds ST on colorectal cancer cells would predictably treat individuals who have metastasized colorectal cancer or who have been identified as being susceptible to metastasized colorectal cancer.
In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as broadly claimed.

In the Reply of 2/12/09, Applicant argues that when the specification is read in its entirety by those skilled in the art, it is apparent that both of the terms "ST receptor" and guanylin cyclase C" are intended to refer to cellular receptors which are referred to by the art recognized, scientifically accepted name "guanylyl cyclase C". Applicant further cites lines 28-34 on page 13 and argues that SEQ ID NO:1 contains the nucleic and amino acid sequence of human guanylyl cyclase C. Applicant further argues that when the cited passage is considered in view of this passage, it is unambiguous that the term "ST receptors" refer to "guanylyl cyclase C" and that the broad interpretation set-forth by the Office is incorrect.

The amendments to the claims and the arguments found in the Reply of 2/12/09 have been carefully considered, but are not deemed persuasive. In regards to the argument that when the specification is read in its entirety by those skilled in the art, it is apparent that both of the terms "ST receptor" and guanylin cyclase C" are intended to refer to cellular receptors which are referred to by the art recognized, scientifically accepted name "guanylyl cyclase C", the broadest reasonable definition is given to the term "guanylyl cyclase C". The specification does not limit the term “guanylyl cyclase C" (disclosed as “guanylin cyclase C”) to a particular SEQ ID NO or to a particular definition found in the art. Rather, at lines 17-20 on page 7, the specification provides the following broad definition:

"As used herein, the term "ST receptor" and "guanylin cyclase C" are interchangeable and meant to refer to the receptors found on colorectal cells, including local and metastasized colorectal cancer cells, which bind to ST."

Said definition is used to define the meaning of "guanylyl cyclase C" in the claims, as Applicant is entitled to be his or her own lexicographer (see MPEP 211.02). Therefore, the term “guanylyl cyclase C" is interpreted to encompass a genus comprising ALL receptors found on colorectal cells which bind to ST.

In regards to the argument the citation of lines 28-34 on page 13 and argument that SEQ ID NO:1 contains the nucleic and amino acid sequence of human guanylyl cyclase C and that when the cited passage is considered in view of this passage, it is unambiguous that the term "ST receptors" refer to "guanylyl cyclase C" and that the broad interpretation set-forth by the Office is incorrect, SEQ ID NO:1 does not comprise an amino acid sequence. Rather, SEQ ID NO:1 is a nucleic acid sequence. Further, with multiple definitions disclosed in the specification, the term "human guanylyl cyclase C protein" is given the broadest definition disclosed in the specification. The broadest disclosed definition is considered the broadest reasonable interpretation. Therefore, "human guanylyl cyclase C protein" is interpreted to encompass any protein receptor found on a colorectal cancer cell which binds to ST.